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**A chemical biology approach to myocardial regeneration.**

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**Public Summary:**

Heart failure is one of the major causes of death in the Western world because cardiac muscle loss is largely irreversible and can lead to a relentless decline in cardiac function. Novel therapies are needed since the only therapy to effectively replace lost myocytes today is transplantation of the entire heart. The advent of embryonic and induced pluripotent stem cell (ESC/iPSC) technologies offers the unprecedented possibility of devising cell replacement therapies for numerous degenerative disorders. Not only are ESCs and iPSCs a plausible source of cardiomyocytes in vitro for transplantation, they are also useful tools to elucidate the biology of stem cells that reside in the adult heart and define signaling molecules that might enhance the limited regenerative capability of the adult human heart. Here, we review the extracellular factors that control stem cell cardiomyogenesis and describe new approaches that combine embryology with stem cell biology to discover drug-like small molecules that stimulate cardiogenesis and potentially contribute to the development of pharmaceutical strategies for heart muscle regeneration.

**Scientific Abstract:**

Heart failure is one of the major causes of death in the Western world because cardiac muscle loss is largely irreversible and can lead to a relentless decline in cardiac function. Novel therapies are needed since the only therapy to effectively replace lost myocytes today is transplantation of the entire heart. The advent of embryonic and induced pluripotent stem cell (ESC/iPSC) technologies offers the unprecedented possibility of devising cell replacement therapies for numerous degenerative disorders. Not only are ESCs and iPSCs a plausible source of cardiomyocytes in vitro for transplantation, they are also useful tools to elucidate the biology of stem cells that reside in the adult heart and define signaling molecules that might enhance the limited regenerative capability of the adult human heart. Here, we review the extracellular factors that control stem cell cardiomyogenesis and describe new approaches that combine embryology with stem cell biology to discover drug-like small molecules that stimulate cardiogenesis and potentially contribute to the development of pharmaceutical strategies for heart muscle regeneration.

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